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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,970	01/11/2002	Rami Lidor-Hadas	1662/55602	3018

26646 7590 02/14/2006

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EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,970	LIDOR-HADAS ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 42-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 42-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 42-51 are pending in the application.

Election/Restrictions

Applicants' election without traverse of Group I in Paper No. 7 was acknowledged in a previous Office Action. The requirement was deemed proper and made FINAL in a previous Office Action.

Rejections made in the previous Office Action that do not appear below have been overcome by Applicants' amendments to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 42-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No persuasive support could be found in the specification or the originally filed claims for "an exo-methylene content of less than **about** 0.01%" as found in claims 1-3 and 42-47 or "an exo-methylene content of less than about **0.1%**" as found in newly added claim 51. Applicants state that support is found on page 3, lines 29-31 and in Example 4 (page 10). In reviewing page 3, lines 29-31, it does identify the exo-methylene as a by-product. However, on lines 23-25

of the same page it states that the exo-methylene by-product is one of the main impurities in ondansetron preparation. Further, Example 4 (page 10) does not state that the product produced has a exo-methylene content of less than **about** 0.01%, which can read on 0.012% 0.015%, 0.019%, etc. In Example 4 it states, "The obtained pure ondansetron hydrochloride dihydrate contained less than 0.01% exo-methylene by-product or undetectable". Therefore, the claims lack written description as such.

Response to Arguments

Applicants' arguments filed November 21, 2005 have been fully considered. Applicants argue that: (1) Example 4 (page 10) supports the current amendment to the claims because Example 4 recites an exo-methylene content of less than about 0.01% level; and (2) with respect to claim 51, the specification describes ondansetron hydrochloride dihydrate having a purity of

at least about 99.9% and such pure ondansetron hydrochloride dihydrate has less than 0.1% impurities including e.g., the exo-methylene by-product (page 2, lines 13-22).

All of Applicants' arguments have been considered but have not been found persuasive. As stated above, Example 4 (page 10) does not state that the product produced has a exo-methylene content of less than **about** 0.01%, which can read on 0.012% 0.015%, 0.019%, etc. In Example 4 it states, "The obtained pure ondansetron hydrochloride dihydrate contained less than 0.01% exo-methylene by-product or undetectable". With respect to newly added claim 51, page 2 does not state that the exo-methylene content is less than 0.1% as found in claim 51. Page 2, lines 13-22 only discusses the purity of the ondansetron hydrochloride dihydrate and not the content of the exo-methylene by-product. Therefore, the rejection is maintained.

Response to Amendment

The Declaration under 37 CFR 1.132 filed February 17, 2005 is insufficient to overcome the rejection of claims 1-3 and 42-50 based upon obviousness under 35 USC § 103 over Chen {Zhongguo Yiyao Gongye Zazhi (1993), 24(6), pages 241-242}, Tyers {U.S. Pat. 4,845,115}, Coates et al. {U.S. Pat. 4,695,578} and Tyers {U.S. Pat. 4,835,173} as set forth in the last Office action because: (1) the Declaration states, not shows, that the prior art does not have a purity of at least about 99.o%, see paragraph 2 on page 1; (2) the Declaration states that the product produced in Coates et al. has 0.12% of the exo-methylene whereas Applicants' claim that their product has less than about 0.1% of the exo-methylene in claim 51, which reads of Coates et al.'s 0.12%, see paragraph 3 of Declaration and instant claim 51; (3) the Declaration fails to show that the instant claimed product has a viable unexpected, unobvious and superior property, not

just of allegedly higher purity; and (4) the Declaration is unclear if the cited prior art were compared with the instant claimed invention, see Table 3, for example.

Further, claims 42-50 are product-by-process claims. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

Since no other ingredient than the Ondansetron hydrochloride dihydrate is present in the

pharmaceutical formulation, claims 45-47 and 50 are interpreted as compound claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 42-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen {Zhongguo Yiyao Gongye Zazhi (1993), 24(6), pages 241-242}, Tyers {U.S. Pat. 4,845,115}, Coates et al. {U.S. Pat. 4,695,578}, Tyers {U.S. Pat. 4,835,173} and Lidor-Hadas et al. {WO 02/36558}, each taken alone or in combination with each other when similar utilities are asserted. An English translation of Chen was provided

with a previous Office Action and will be referred to hereinafter.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicants claim Ondansetron hydrochloride dihydrate. Each of Chen {page 1, Compound (1) and page 2- section III}, Tyers '115 {column 3 and especially Example 2 in column 3}, Coates et al. {column 4 and especially Example 10 in column 20}, Tyers '173 {column 3 and especially Example 2 in column 3} and Lidor-Hadas et al. {page 3, lines 12-21 - Form A} teach Ondansetron hydrochloride dihydrate.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claimed invention and the prior art is that the prior art is silent as to the purity of the product obtained.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Changing the form, purity, color, or other characteristic of an old product without a new use as a result thereof does not render product patentable where utility remains the same. *Ex parte Hartop*, 139 USPQ 525. The compounds are of the same identical formula and as such would be expected to have the same utility. The difference, if any, may reside in there being of a higher purity.

One of ordinary skill in the art would be motivated to prepare a purer form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected, unobvious and superior property (not just an alleged higher

purity), the instant claimed invention is found obvious over the cited prior art.

Response to Arguments

Applicants' arguments filed November 21, 2005 have been fully considered. Applicants argue that: (1) all of the cited prior art teach the same inferior process for preparing Ondansetron hydrochloride dihydrate; (2) in Exhibit B, the process in Coates has been repeated to provide exemplary data for this inferior process and the instant claims have been amended to circumvent that 0.12% impurity content of Coates; (3) there are other factors besides utility which must be considered when determining obviousness and cites *In re Cofer*, 354 F.2d 664, 667-668 (C.C.P.A. 1966); (4) the Office Action fails to provide any evidence why the claimed product would be obvious over the prior art; and (5) the prior art does not suggest suitable methods of obtaining the pure compound.

All of Applicants' arguments have been considered but have not been found persuasive. Applicants claim Ondansetron hydrochloride dihydrate. Chen, Tyers '115, Coates et al., Tyers '173 and Lidor-Hadas et al. each teach Ondansetron hydrochloride dihydrate. Applicants argue that all of the cited prior art teach the same inferior process for preparing Ondansetron hydrochloride dihydrate. In response, Applicants are claiming a product, not a process of making. Further, Applicants have not persuasively demonstrated factually that the cited prior arts' compounds are inferior. Applicants argue the data found in Exhibit B. In response, an Exhibit B was not found with the submission of November 21, 2005. However, if Applicants are referring to the Declaration under 37 CFR 1.132 filed February 17, 2005 as Exhibit B, the showing was found insufficient for reasons stated above.

Applicants argue that other factors besides utility must be considered when determining obviousness and that the Office Action fails to provide any evidence why the claimed product would be obvious over the cited prior art. In response, all of the cited prior art, except Chen, teach a recrystallization step when preparing the Ondansetron hydrochloride dihydrate. Since recrystallization is a process for purifying a compound, one skilled in the art would expect the obtain product to be of a high purity. It has long been the practice in the chemical and pharmaceutical arts to produce pure compounds since a compound such as Ondansetron hydrochloride dihydrate, which is known to treat depression, would be administered orally, transdermally, etc. Purer forms of known products may be patentable, but the mere purity of a product, by itself, does not render the product unobvious. *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). Applicants have not persuasively demonstrated that the

instant claimed compounds have enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc.

Applicants argue that the prior art does not suggest suitable methods of obtaining the pure compound. In response, products are under examination in the instant application and not processes of making. For all the reasons given above, the rejection is deemed proper and is maintained.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the

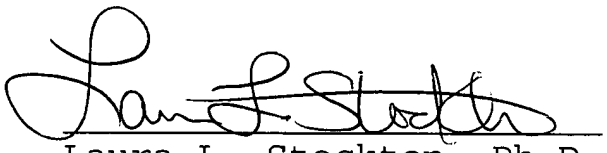
mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information

Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.



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February 8, 2006